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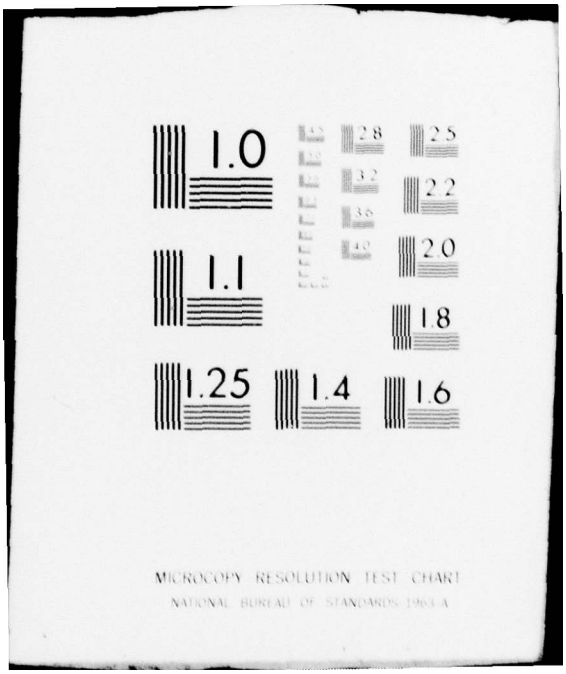
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HEMOGLOBIN FUNCTION IN STORED BLOOD

Annual Report

January 1979

(for the period 1 February 1978 - 31 January 1979)

by

R. Ben Dawson, M. D.

Supported by

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University of Maryland School of Medicine
Baltimore, Maryland 21201

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

This report presents ATP, 2,3-DPG, pH, and glucose levels of whole blood and packed cells stored in CPD-adenine with the following variables; pH, glucose concentrations, adenine, inosine, methylene blue, phosphate, pyruvate, dihydroxy-acetone, ascorbic acid, fructose, mannose, galactose, and ribose. Also, D-ascorbate, dehydroascorbate and SH inhibitors.

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HEMOGLOBIN FUNCTION IN STORED BLOOD

February 1, 1978 thru January 31, 1979

INTRODUCTION

During this contract year, work was continued on liquid preservation of stored blood for the purpose of maintaining 2,3-DPG levels for hemoglobin function and ATP levels for red cell post transfusion survival. Preservatives used were CPD (citrate-phosphate-dextrose), and CPDA-1. Other variables studied were concentrations of glucose, other 5 and 6 carbon sugars and three dissaccarides. Also, the metabolic regulators, methylene blue and ascorbate, D-ascorbate and dehydroascorbate, with sulfydryl inhibitors. Other experiments used concentrations of phosphate, dehydroxyacetone, inosine and adenosine.

This report covers 11 months of contract work during which time 16 experiments were brought to completion. Some of these will not be covered in this report as data analysis is not complete on several. The 16 items given as the body of this report include the abstract of a previously submitted paper and abstracts submitted for publication on three of the papers whose entire manuscripts are given herein. Thus, in the 11 abstracts which are in this report, 7 give results not given previously or in this report; and, in addition there are 5 manuscripts submitted here for the first time.

RESULTS AND DISCUSSION

One of the important conclusions from our large, CPD-adenine packed cell study, Blood Preservation 26, is that high hematocrit packed cells (Hct 80-95%) require at least 175% of the glucose present in CPD for 35 days of storage. Also, for 42 days of storage, 200% of glucose seems to be indicated.

In BP 28, galactose and maltose were shown to be of some value in maintaining red cell 2,3-DPG and ATP, although not as good as fructose and dextrose.

In BP 33, phosphate, in increased concentrations was shown to have a beneficial effect on 2,3-DPG levels with ribose as well as inosine. This is a new finding and adds some impetus to the exploration of alternate sugars to glucose such as ribose.

Dihydroxyacetone (DHA) has been of some interest for 5 years, for its ability to maintain 2,3-DPG although its adverse effect on ATP has been a concern. In BP 34, increasing the phosphate concentration reduces the adverse effect of DHA on ATP. The extra phosphate, 10 mM, slightly lowers 2,3-DPG values; however, the levels are still maintained at approximately half normal for 4 weeks. The merit of this 2,3-DPG maintenance in a DHA-10 mM phosphate preservative, that maintains higher than control ATP values, should be further evaluated.

In another experiment, BP 35, DHA and D-ascorbate were evaluated together with phosphate in CPD-adenine. Again, ATP maintenance was improved with DHA and phosphate. However, DHA and D-ascorbate kept 2,3-DPG levels above normal for 6 weeks of storage. As in the experiments without ascorbate, phosphate improved ATP maintenance in DHA with ascorbate.

Our first experiment in the reevaluation of adenosine is reported here in abstract form, BP 40. 5 mM adenosine maintained 2,3-DPG at near normal for 21 days of storage and was clearly better than lower concentrations. However, ATP concentrations were depressed by adenosine. Of note was the higher glucose levels observed with this 5 mM preservative, possibly indicating glucose sparing as the ribose part of adenosine is utilized. BP 41 studied adenosine in a CPD-adenine

RESULTS AND DISCUSSION (CONT)

preservative with D-ascorbate. Although the adverse effect noted above adenosine on ATP is additive to the adverse effect of D-ascorbate, there is an important additive effect of adenosine and D-ascorbate on 2,3-DPG maintenance

In further studies on the ascorbic acid mechanisms of red cell maintenance of 2,3-DPG, BP 43, iodoacetate was shown to have a profound inhibitory effect on red cell metabolism, not protected by ascorbate or glutathione. In BP 44, dehydro-ascorbate, the oxidized form of the redox pair, was shown to have a slightly greater ability to maintain 2,3-DPG during blood storage than D-ascorbate, the unnatural isomer of the vitamin.

The ion exchange resin, Amberlite-45 with and without phosphate, was shown to stabilize blood preservative pH during storage in CPD, helping to maintain 2,3-DPG. Also, the phosphate loaded resin was presumed to release phosphate slowly during storage, thus facilitating maintenance of ATP.

Passage of oxygen through the plastic blood storage bag has been shown to raise the partial pressure of oxygen during liquid blood storage. It is supposed that a resultant increase in the fraction of oxyhemoglobin will release bound 2,3-DPG, thus inhibiting the formation of more 2,3-DPG during blood storage. The quantitative impact of this effect of gas permeable plastic blood bags is being assessed.

SUMMARY

With the licensing of CPDA-1 for 5 weeks of blood bank storage in Aug. 1978 and the adoption of this advance by the American National Red Cross in September, a major development in blood preservation research has been realized. The next major effort in this field; that is, maintaining normal 2,3-DPG levels for immediate oxygen transport upon transfusion now comes to the front among the unresolved issues in blood preservation and transfusion therapy. As this work has been going on, studies in animals and humans has shown improved function and survival when higher or normal 2,3-DPG blood is transfused, compared to the low 2,3-DPG blood, in certain control circumstances.

The present report summarizes the results of 11 abstracts and 5 manuscripts most of which are directly aimed at maintaining 2,3-DPG levels over 5-6 weeks of blood bank storage. The 5 manuscripts and 7 of the abstracts represent work not previously reported. Four of the abstracts are on work presented in part, previously. This laboratory expects to continue this work with some of the metabolic regulators and nutrients mentioned here and others as well.

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